A5

34. (Amended) A nucleic acid coding for an essential secretory gene for Helicobacter, identified by the method as claimed in claim 22.

35. (Amended) A gene library comprising at least two nucleic acids claimed in claim 34.

A6

44. (Amended) A polypeptide characterized in that it is encoded by nucleic acid as claimed in claim 34.

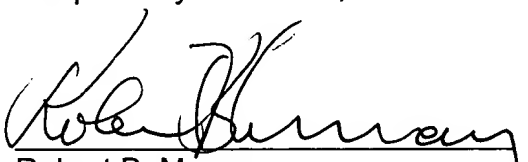
A7

50. (Amended) The use of a polypeptide or of a fragment thereof as claimed in claim 44 thereof as immunogen for generating antibodies.

REMARKS

Claims 1-58 are pending in this application. By this Amendment, claims 4,5, 8-12, 15-19, 21, 29, 32, 33, 34, 38, 39, 44, 50 are amended to correct the multiple dependency thereof and to place this application into better condition for examination. No new matter is added.

Respectfully submitted,



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Claims

1. A method for providing agents for the detection, for the prevention or/and for the therapy of microbial infections,

characterized in that

it comprises the steps:

(A) identification of essential genes and the corresponding polypeptides by producing gene-deficient microorganisms by conditional antisense inhibition (CAI) or/and subtractive recombination mutagenesis (SRM) and determining the viability or/and survivability of the gene-deficient microorganisms in an assay system.

(B) identification of specific active ingredients which are directed against the essential polypeptides and bring about inactivation of the microorganisms or used microorganisms.

(C) testing of the identified active ingredients for their usability as components of diagnostic, preventive or/and therapeutic compositions,

(D) formulation of the useful active ingredients as diagnostic, preventive or/and therapeutic compositions.

2. A method as claimed in claim 1,

characterized in that

obligately essential genes are identified by CAI.

3. A method as claimed in claim 1,

characterized in that

facultatively essential genes are identified by SRM.

4. A method as claimed in ~~any of the preceding claims~~ claim 1,

charact riz d in that

step (A) is preceded by selection for genes which code for polypeptides having a particular functionality or/and which code for polypeptides which are expressed in a particular stage of development.

5. A method as claimed in ~~any of the preceding claims~~ claim 1, characterized in that the selection is carried out with the aid of hybridization methods selected from subtraction and array methods.

6. A method as claimed in claim 5, characterized in that the selection is carried out for specific subtracted apathogenic or pathogenic genes.

7. A method as claimed in claim 5, characterized in that the selection is carried out for specific subtracted genes of *H. pylori* or *H.heilmannii*.

8. A method as claimed in ~~any of claims 4 to 7~~ claim 4, characterized in that gene sequences coding for exported polypeptides are selected.

9. A method as claimed in ~~any of claims 4 to 8~~ claim 4, characterized in that gene sequences coding for secreted polypeptides are selected.

10. A method as claimed in ~~any of claims 4 to 9~~ claim 4, characterized in that genes which code for polypeptides and which are necessary for the development of the vital form from the resistant form are selected.

11. A method as claim d in ~~any of claims 4 to 9,~~ claim 4,
characterized in that
genes which code for polypeptides and which are necessary for development of the resistant form from the vital form are selected.

12. A method as claimed in ~~any of the preceding claims~~ claim 1,
characterized in that
in step (A) test systems selected from *in-vitro* systems, cell culture systems, tissue culture systems and animal models are used as natural environment for determining the viability and survivability of the gene-deficient microorganism.

13. A method as claimed in claim 12,
characterized in that
the deficient gene sequences which lead to gene-deficient microorganisms which are not culturable and incapable of survival in the natural environment are assigned to the category of obligately essential genes.

14. A method as claimed in claim 12,
characterized in that
the deficient gene sequences which lead to gene-deficient microorganisms which are culturable but incapable of survival in the natural environment are assigned to the category of facultatively essential genes.

15. A method as claimed in ~~any of the preceding claims~~ claim 1,
characterized in that
the identified genes are used to produce primers with whose aid corresponding genes from related microorganisms, subspecies or/and species are identified.

16. A method as claimed in ~~any of the preceding claims~~ claim 1,
characterized in that

in step(B) there is identification of specific active ingredients which influence the expression, pr sentation and/or function of the essential polypeptides, in particular immunologically active substances, binding partners of the polypeptides or fragments thereof or/and inhibitory substances.

17. A method as claimed in claim 1 ~~any of the preceding claims~~,
characterized in that
step(B) comprises a determination of the immunogenic potential of the polypeptides or/and fragments thereof, with the identified genes being expressed and subsequently a Western blot analysis being carried out or/and in that the identified polypeptides or fragments thereof are used to carry out a vaccination in cell culture or in an animal model, and the induction of a specific immune response is observed.

18. A method as claimed in claim 1 ~~any of the preceding claims~~,
characterized in that
step (B) comprises a determination of the binding potential of the polypeptides or fragments thereof by screening of substance libraries, surface display methods, crystallographic analysis or/and computer modelling.

19. A method as claimed in claim 1 ~~any of the preceding claims,~~
characterized in that
the diagnostic, preventive or/and therapeutic agents are provided in the form of passive vaccines or active vaccines.

20. A method as claimed in claim 19,
charact rized in that
the passive vaccines are provided in the form of antibodies or/and antibody fragments and the active vaccines are provided in the form of heterologous carrier systems or/and in the form of antigens or antigen fragments, subunit vaccines, live vaccines, DNA vaccines or/and food vaccines.

21. A method as claimed in ~~any of the preceding claims 1 to 19~~ Claim 1,
charact rized in that
the diagnostic, pr ventive or/and therapeutic agents comprise inhibitory substances, in particular expression inhibitors or/and enzyme inhibitors.

22. A method for identifying essential microbial genes,
characterized in that
it comprises the steps:
(i) production of gene-deficient microorganisms,
(ii) determination of the viability or/and survivability of the gene-deficient microorganisms from (i),
(iii) identification of a protein-encoding section of a microbial DNA sequence in which the gene-deficient microorganisms are deficient.
(iv) Characterization of those DNA sections which are essential for survivability.

23. A method as claimed in claim 22,
characterized in that
the gene-deficient microorganisms are produced by mutagenizing a DNA section in a microbial genome.

24 A method as claimed in claim 22,
characterized in that
the DNA section is mutagenized by transposon mutagenesis.

25. A method as claimed in claim 23,
characterized in that
the mutagenization of the DNA section on the microbial genome takes place by homologous recombination.

26. A method as claimed in claim 25,
charact riz d in that
the SRM method is used.

27. A method as claimed in claim 23,
characterized in that
the gene-deficient microorganisms are produced by expressing a DNA section or a part-sequence thereof in the form of antisense RNA in microorganisms.

28. A method as claimed in claim 27,
characterized in that
the CAI method is used.

29. A method as claimed in ~~any of claims 22 to 28~~ claim 22,
characterized in that
test systems selected from *in-vitro* systems, cell culture systems , tissue culture systems and animal models are used as natural environment to determine the viability or/and survivability of the gene-deficient microorganisms.

30. A method as claimed in claim 29,
characterized in that
the deficient gene sequences which lead to gene-deficient microorganisms which are not culturable and incapable of survival in the natural environment are assigned to the category of obligately essential genes.

31. A method as claimed in claim 29,
characterized in that
the deficient gene sequences which lead to gene-deficient microorganisms which are culturable but incapable of survival in the natural environment are assigned to the category of facultatively essential genes.

32. A method as claimed in ~~any of claims 22 to 31~~ claim 22,
characterized in that

the identification of the protein-encoding DNA section takes place by expression in a host organism and detection of the presence of an expression product.

33. A method as claimed in ~~any of claims 22 to 32,~~ claim 22
characterized in that
it additionally comprises:

(v) production of primers for amplification and detection of homologous gene sequences in heterologous microorganisms

(vi) identification of the homologous gene sequences.

34. A nucleic acid coding for an essential secretory gene from *Helicobacter*, identified by the method as claimed in ~~any of claims 22 to 33~~. claim 22,

35. A nucleic acid as claimed in claim 34,
characterized in that
it codes for a secreted polypeptide with signal peptide.

36. A nucleic acid as claimed in claim 34,
characterized in that
it codes for a secreted polypeptide without signal peptide.

37. A nucleic acid
characterized in that
it comprises

(a) one of the nucleic acid sequences depicted in SEQ ID NO: n, where n is an odd integer from 1 to 245 inclusive, or a protein-encoding section thereof,

(b) a nucleotide sequence corresponding to one of the sequences from (a) within the scope of the degeneracy of the genetic code or

(c) a nucleotide sequence hybridizing with one of the sequences from (a) and/or (b) under stringent conditions.

38. A gene library comprising at least two nucleic acids as claimed in ~~any of~~ claim 34 ~~claims 34 to 37~~.

39. A vector
characterized in that
it comprises at least one nucleic acid as claimed in ~~any of claims 34 to 37~~ claim 34 or a section thereof.

40. A vector as claimed in claim 39,
characterized in that
it is a CAI vector.

41. A vector as claimed in claim 39,
characterized in that
it is an SRM vector.

42. A cell,
characterized in that
it is transformed with a nucleic acid as claimed in any of claims 34 to 37 or a vector as claimed in any of claims 39 to 41.

43. A mutant library
characterized in that
it consists of at least two microorganisms transformed with a vector as claimed in claim 40 or with a vector as claimed in claim 41.

44. A polypeptide
characterized in that
it is encoded by a nucleic acid as claimed in ~~any of claims 34 to 37.~~ claim 34

45. A polypeptide as claimed in claim 44,
characterized in that

it comprises

(a) one of the amino acid sequences depicted in SEQ ID NO: m, where m is an even integer from 2 to 246 inclusive, or

(b) a sequence which cross-reacts immunologically with one of the sequences according to (a).

46. A polypeptide as claimed in claim 45,
characterized in that
it is an essential secreted polypeptide.

47. A polypeptide fragment,
characterized in that
it has an immunogenic section of one of the sequences claimed in claim 45.

48. An inhibitory molecule obtainable by the method as claimed in claim 1,
characterized in that
it is able to bind specifically to a polypeptide or fragment thereof as claimed in any of claims 44 to 47 or/and to influence the expression, presentation or/and natural function thereof.

49. A method for producing a polypeptide or polypeptide fragment as claimed in any of claims 44 to 47
characterized in that
a cell is transformed with a nucleic acid as claimed in any of claims 34 to 37 or with a vector as claimed in claim 39, the transformed cell is cultivated under conditions with which expression of the polypeptide takes place, and the polypeptide is isolated from the cell or/and the culture supernatant.

50. The use of a polypeptide or of a fragment thereof as claimed in ~~any of claims 44 to 47~~ claim 44 thereof as immunogen for generating antibodies.

51. An antibody or fragment thereof,

charact riz d in that

it is specific for a polypeptid or a fragment thereof as claimed in any of claims 44 to 47.

52. A pharmaceutical composition,

characterized in that

it comprises as active ingredient

a) a nucleic acid as claimed in any of claims 34 to 37,

b) a vector as claimed in claim 39,

c) a cell as claimed in claim 42,

d) a polypeptide or a fragment thereof as claimed in any of claims 44 to 47,

e) an antibody or fragment thereof as claimed in claim 51 and/or

f) an inhibitory molecule as claimed in claim 48

where appropriate together with conventional pharmaceutical excipients, diluents, additives and carriers.

53. The use of a pharmaceutical composition as claimed in claim 52 for the diagnostic, prevention or/and therapy of a *Helicobacter* infection.

54. The use of a pharmaceutical composition as claimed in claim 52 for inhibiting the reproduction of *Helicobacter* oganisms and/or other anthrogenic microorganisms in a host.

55. The use as claimed in claim 54,

characterized in that

a nucleic acid as claimed in any of claims 34 to 37 is formulated as DNA vaccine.

56. The use as claimed in claim 54,

characterized in that

a polypeptide or polypeptide fragment as claimed in any of claims 44 to 47 is formulated as subunit vaccine or as live vaccine.

57. The use of a pharmaceutical composition as claimed in claim 52 for producing an agent for the diagnostic, prevention or/and therapy of a *Helicobacter* infection.

58. A vector as claimed in claim 41,
characterized in that
the SRM vector is the vector pSRM4 (SEQ ID No. 247).